iron in the diet and so improve the anæmia. Evidently the hæmatinic effect of the acid is so slight as to be of no therapeutic value in this disease. Achlorhydria or *an associated deficiency in gastric secretion* may be the contributing factor in the causation of the nutritional anæmias, while diet deficiency is apparently the most common precipitating causative factor.

SUMMARY AND CONCLUSIONS

The negative results of the HCl treatment by mouth in cases of nutritional anæmia in children are reported and the relationship of achlorhydria to the causation of this type of anæmia is discussed.

The cases from the Hospital for Sick Children, London, were studied through the courtesy of Drs. Donald Paterson and E. A. Cockayne, and those observed at St. Paul's, Vancouver, through permission of Dr. A. H. Spohn. I wish to express my gratitude to Drs. A. G. Signy and W. W. Payne for assistance with the laboratory procedures, and to John Wyeth & Brother for supplying therapeutic iron.

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THE SIGNIFICANCE OF INDIGO, CYANOGEN AND THIOCYANATE IN TUMOUR CASES*

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IT was shown in a previous paper[1] that indigo occurs in the veins of rabbits. In the liver, in the vena cava and its branches, in the veins of the stomach, intestines and mesentery, the indigo was found to exist in a leuco form, and its detection depended upon oxidation to the blue form. As similar normal human tissues were not available, it is assumed that the indigo in these also exists in the leuco form. In view of the proposed explanation of the function of indigo that follows, it seems probable that it should exist in the leuco form in normal healthy internal organs, and that it would not be found in the blue form except in diseased conditions. Human tissues were available from malignant tumours of the liver and of abdominal lymph nodes. The indigo in the veins of these tumours was already in the blue form so that oxidation was an unnecessary part of the procedure for its detection.

In the paper referred to it was also shown that the indigosulphonates held calcium in a state of supersaturation in a phosphate-containing Ringer's solution. Consequently, it was suggested that the state of calcium supersaturation in most of the body fluids might also be due to the presence of indigo in the veins and capillaries. Such a function would seem secondary, and its primary function would seem more likely to depend upon its reversible oxidation-reduction properties. This view finds support in the fact that it has been found in the two forms, leuco in the veins of the liver and other abdominal organs of normal rabbits, blue in the veins of tumours of the liver and other human abdominal organs. It was probably found in the blue form because it had lost its ability to be reduced to the leuco form. The change from the more soluble leuco form to the less soluble blue form is probably part of a defensive mechanism in cases of accident to prevent loss of blood to the tissues in order to provide sufficient circulation in the brain to maintain consciousness. Such a defensive mechanism might operate in other emergencies like that of the rat described below. In all cases its efficiency would depend upon its complete reversibility. Should conditions be such that the less soluble blue form did not revert completely back to the more soluble white form, then it would gradually fill the vein and capillary walls and render them less permeable to the passage of oxygen and nutritive material. The resulting condition of the tissues would be quite comparable to that produced by ligating the inferior blood supply to the uterus of a rat.[2] The consequent malnutrition of the rat uterus would constitute a call for help that would probably be answered by the indigo mechanism in the veins and capillaries of the closely related mammary gland limiting diffusion of nutrition there in order to make more available

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for the starving uterus. As the emergency continued, the uterus appeared to absorb nutrition from the intestines, which became obstructed by the resulting hardened fæces, which caused the rat's death before the tumour had a chance to develop. The undernourished mammary gland having no such recourse as that afforded the uterus consequently succumbed to tumour much more often.

Such a mammary gland tumour developed in a rat following the ligation of the inferior blood supply to both horns of the uterus. When the rat died at 30 months of age its tumour weighed more than the rest of its body. This tumour was observed during its 12 months' growth and tested repeatedly for the occurrence of gases. A large hypodermic needle and syringe were used for this purpose. The syringe was provided with a stopcock to prevent loss or contamination of contents when the needle was withdrawn. The syringe was partly filled with water so that the presence of any gas withdrawn might be indicated by bubbles. No gas was ever found in the interior of the tumour, which autopsy showed was not necrotic. Small pockets of gas were located between the lobes and within the periphery. Negative pressure within the syringe caused the gas to bubble through the water, in which it seemed readily soluble. The tests applied indicated the presence of ammonia and cyanogen. Later probings were made chiefly to detect cyanogen so weak potassium hydroxide was used instead of water, and the Prussian blue and ammonium sulphide tests[3] applied immediately. The respective green and red colorations obtained indicated the presence of cyanide.

Experimentally produced tumour in a rat was not unique in harbouring cyanogen. It was also found in an obstructed loop of a dog's intestine and in a spontaneously occurring mammary gland tumour of another dog It was also found in the following human case:

E.B. was a woman 39 years of age whose history showed the removal of the left breast on account of carcinoma. A few months later, when the other breast also appeared cancerous, she came to a cancer clinic where tests were made for cyanogen. Her right breast was probed to locate a pocket of gas, which was withdrawn into potassium hydroxide and gave the tests for cyanide.

Thiocyanate is a recognized constituent of normal human urine.[4] It is found in increased quantities in certain degenerative diseases including cancer. It was found in increased quantities by the authors in cases of gastrointestinal tumour. The average daily excretion of thiocyanate determined by the Baumann method[5] greatly exceeded that found by Baumann for his normal cases, but the individual determinations varied considerably, due, probably, to corresponding variations in the amount of cyanogen that was excreted otherwise. The source of thiocyanate has long remained unknown, but it is generally considered to be cyanogen formed as a by-product of cellular metabolism or katabolism. It is likely washed out of actively metabolizing cells by incoming oxygen and outgoing carbon dioxide, and under normal conditions is probably eliminated quickly, partly by way of the skin and lungs and partly as thiocyanate in the urine.

Cyanogen is probably formed more in tumour than in normal tissues, and, when formed, probably finds it harder to escape from tumour than from normal tissue. Its escape is probably rendered difficult on account of the decreased permeability not only of tumour tissue but also of its veins and capillaries. The delayed elimination of cyanogen would tend to divert some of it into intercellular spaces and lymph channels along which it would make its way until hindered by some obstruction that would cause it to collect in pockets such as found. When so delayed, it would probably unite with the oxygen catalyst[6] and thus bring about the lowered oxygen consumption and malnutrition of the affected tissues that might result in a general cancerous condition or in definite tumour growth. If the pocket of gas were formed on the outskirts of the tumour, the new growth initiated would but add to the size of the old. This is probably what happened in the case of the rat, but the removal of some of the cyanogen probably delayed the rapidity of the growth and thereby prolonged the rat's life. If, however, the gas were not trapped until some distance from the original tumour, the new growth would constitute what is generally regarded as a metastasis.

CONCLUSIONS

From the foregoing considerations the following conclusions seem justified:

1. The existence of indigo blue in the veins of internally occurring tumours seems to indicate that continuance in its less soluble form may be responsible for initiating the growth of such

tumours by making the vein and capillary walls of that area less permeable to oxygen and nutritive material and thus bringing about the malnutrition of the tissues that when experimentally produced in rats resulted in tumour.

2. The existence of cyanogen in tumours seems to indicate that its known action on the oxygen catalyst probably causes a continuation of the deficiency of oxygen initiated by the indigo, and would thus be responsible not only for increased growth at the original site but also for metastases at more distant sites to which it might have escaped.

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A TUBERCULOSIS SURVEY OF MANITOBA INDIANS*

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THE Sanatorium Board of Manitoba, with the authorization of the Department of Indian Affairs, undertook in 1937 a tuberculosis survey of Indian Reserves and Indian Residential Schools of Manitoba. The work had to be fitted into the usual busy program of clinics among the white communities but by Fall six reserves and seven residential schools had been surveyed.

In all, 2,672 Indians were examined, of whom 1,856 were on reserves and 816 in schools. A complete survey of each school was made; but on the reserves it was not possible to examine everyone, for in each instance various activities such as hunting, fishing and visiting took a number away. However, an effective method of attack and splendid cooperation usually resulted in an almost complete turnout of all at home, so that a good cross-section of each reserve was obtained, with the sexes equally divided and ages ranging from one year to over one hundred. The average clinic attendance for each reserve was 75 per cent of the total population. About one-fifth of the 15,000 Indians in the province live on the reserves that were surveyed. Inasmuch as approximately half of Manitoba's Indians live in the hinterland it may be considered that the present survey represents about two-fifths of the total Indian population who have any significant contact with white communities.

The opinion that Indian tuberculosis is a menace to white people is widely held and would seem well founded, and has certainly been a potent factor in the present campaign for investigation. Yet it has not been based altogether on statistical evidence, and a brief study of the tuberculosis death rates of four reserves in this survey compared with those of the adjacent communities gives rather surprising results. The average death rate for the reserves is 1,020 per 100,000, while that of the surrounding municipalities is 51 per 100,000, which is definitely lower than the whole death rate of 59 per 100,000 for the province, including Indians. In the case of the Oak River Reserve, where the surrounding population contains few half-breeds, the rates are respectively 727 per 100,000 and 26 per 100,000. These figures, though not conclusive, are interesting in view of the general opinion that reserves are a menace to surrounding communities.

The purpose of this survey was primarily to ascertain accurately the incidence of tuberculosis infection and disease among the Treaty Indians. Upon this point there has been endless speculation but no statistical knowledge to temper the impression that the Indian was still overwhelmingly scourged by the disease. Identification of those suffering from tuberculosis was a further aim. Finally, it was hoped that the data compiled would serve as a foundation for a future program of prevention and treatment.

In choosing the reserves for survey we were influenced by accessibility, which also usually meant proximity to white populations, by the interest and expected cooperation of the doctor

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